AMENDMENTS TO THE SPECIFICATION

In the specification:

Amendments to the specification are provided in the substitute specification, marked and unmarked copies of which are filed herewith, along with a Statement That the Specification Contains No New Matter. The amendments to the specification also include the amendment to the priority claim made by the Preliminary Amendment mailed December 8, 2003.

On page 204, after the text and before the claims, please enter the sequence listing provided herewith (40 pages) and renumber the pages with the abstract and the claims accordingly.

AMENDMENTS TO THE CLAIMS

Please amend claims 3, 25, 54-56, 58, 59, 62-64, 91 and 92, and cancel claims 9-14, 16, 17, 19-22, 28-35, 37-51, and 65-89, as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application. Please cancel claims 9-14, 16, 17, 19-22, 28-35, 37-51, and 65-89 without prejudice to their pursuit in an appropriate divisional or continuation application. Claims 1-8, 15, 18, 23-27, 36, 52-64, and 90-92 are pending in the application.

In the claims:

1. (original) Use of a compound of general formula I, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament.

2. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament for the treatment of arrhythmia.

3. (currently amended) Use according to ~~the preceding claim~~claim 2, where said arrhythmia is a reentry arrhythmia of either atrial or ventricular origin, including repolarisation alternans arrhythmia where both supraventricular and ventricular tachyarrhythmias may present as tachycardia, flutter or fibrillation.

4. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament for prevention and/or treatment of slowed conduction in the heart.

5. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament for improvement of contractility of the heart.

6. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament for treatment of disease

states associated with impaired GJIC during metabolic stress, including glucose and oxygen deprivation.

7. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament for antithrombotic treatment.

8. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 for the preparation of a medicament useful in prevention and /or treatment of osteoporosis.

9. – 14. (canceled)

15. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 that increase gap junctional coupling and/or GJIC in the vascular wall for the preparation of a medicament for the prevention and/or treatment of hypertension.

16. – 17. (canceled)

18. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 herein for the preparation of a medicament useful in prevention and /or treatment of deafness associated with impaired GJIC.

19. – 22. (canceled)

23. (original) Use of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 herein for the preparation of a medicament useful in improving glucose tolerance in a subject with non-insulin dependent diabetes mellitus due to impaired GJIC between β-cells.

24. (original) A method of treatment of arrhythmia comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8.

25. (currently amended) A method of treatment according to ~~the preceding claim~~ claim 24, wherein said arrhythmia is a reentry arrhythmia of either atrial or ventricular origin, including repolarisation alternans arrhythmia where both supraventricular and ventricular tachyarrhythmias may present as tachycardia, flutter or fibrillation comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of general formula 1, formulae I to VIII, formulae 2 to 12, and the compounds of tables 1 and 8.

26. (original) A method of increasing the gap junctional intercellular communication of mammalian cells subjected to glucose and/or oxygen deprivation comprising administering an effective amount of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8.

27. (original) A method of antithrombotic treatment comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8.

28. – 35. (canceled)

36. (original) A method of treating or preventing hypertension by increasing gap junctional coupling and/or GJIC in the vascular wall comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8.

37. – 51 (canceled)

52. (original) A method of preventing or treating a non-proliferative disease comprising administering a therapeutically effective amount of a compound that facilitates intercellular communication as determined by effect in the $CaCl_2$ arrhythmia mouse model.

53. (original) A method according to claim 52 wherein said compound has a score in said mouse model of 2 or 3.

54. (original) The method of claim 52 wherein said compound facilitates gap junctional intercellular communication.

55. (currently amended) The method of ~~claims 52-54~~claim 52 wherein said compound is an agonist of an antiarrhythmic peptide receptor.

56. (currently amended) The method of ~~claims 52-55~~claim 52, wherein said compound is selected from the group consisting of resveratrol including including the various isomers, dimers, trimers, tetramers and derivatives thereof.

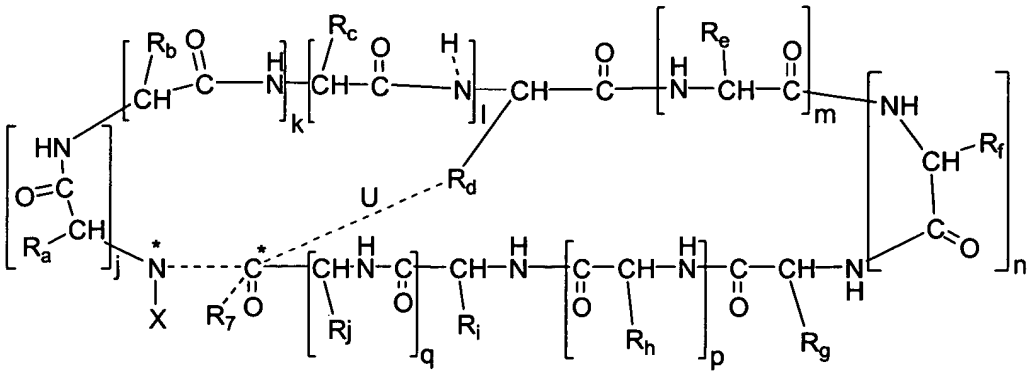
57. (original) The method of claim 56, wherein the compound is trans-resveratrol (trans-3,5,4'-trihydroxystilbene).

58. (currently amended) The method of ~~claims 52-54~~claim 52, wherein said compound is a selected from the group consisting of irsogladine or (6-(2,5-dichlorophenyl)-2,4-diamino-1,3,5-triazine) and derivatives thereof.

59. (currently amended) The method of ~~claims 52-54~~claim 52, wherein said compound is selected from the group consisting of the aporphinoid alkaloids, preferably boldine and taspine and derivatives thereof.

60. (original) A method of preventing or treating a disease characterized by decreased GJIC in the diseased tissue comprising administering a therapeutically effective amount of a compound that facilitates intracellular communication as determined by effect in the calcium chloride arrythmia mouse model, wherein said compound is selected from the group of compounds having the formula I:

(I)



representing a peptide sequence wherein the amino acid residues may be D- and/or L-forms, and having the N-terminal at N* and the C-terminal at C* and being optionally cyclic via a covalent bond between N* and C* as shown by a broken line or between R_d and C* as shown by the broken line U; the broken line between N* and C*, which when present excludes the bond U, represents an optional covalent bond and when said bond is not present then N* is bound to a hydrogen atom; when the optional covalent bond U between Rd and C* is present then R7 is void and the presence of R7 excludes the bond U;

and wherein

X represents an N-terminal moiety such as a photoprobe capable of being bonded to the amino terminal N*, or an acyl group derived from a C(2-22)alkyl carboxylic acid, such as acetic acid, propionic acid, butyric acid and other fatty acids, such as behenic acid, optionally substituted with one or more substituents selected from the group consisting of hydroxy, halogen, C(1-6)alkyl, nitro and cyano; or X represents hydrogen;

R_7 represents OH, NH_2, $NHNH_2$, NHR_8 or OR_8 when the bond between N* and C* is missing, or R_7 is absent when there is a bond between N* and C*;

R_8 represents H or a straight or branched C(1-6)alkyl group, an aryl or an aralkyl group.

R_a represents the amino acid side chain of Hyp or Pro;

R_b represents the amino acid side chain of Hyp or Pro;

R_c represents the amino acid side chain of Gly, Sar, an aromatic amino acid side chain optionally substituted with one or more hydroxy, halogen, nitro, cyano, azido, amino, benzoyl or lower alkoxy or thioalkoxy group in the aromatic ring;

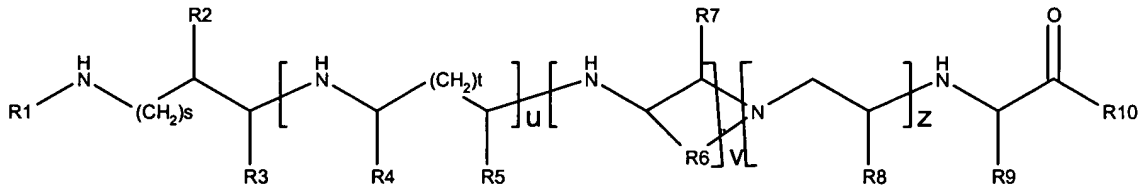
R_d represents the amino acid side chain of Ala, Gly, Glu, Asp, Dab, Dapa, Lys, Asn, Gln, Orn, Thr, Ser or Cys;

R_e represents the amino acid side chain of Ala;

R_f represents the amino acid side chain of Ala, Sar or Gly;
R_g represents any amino acid side chain except the side chain of L-4Hyp or a moiety of formula Z or Za;
R_h represents the amino acid side chain of Ala, or R_g represents a moiety of formula Z or Za;
R_i represents the amino acid side chain of Gly or R_i represents an aromatic amino acid optionally substituted with one or more hydroxy, halogen, nitro, cyano, azido, amino, benzoyl or lower alkoxy or thioalkoxy group in the aromatic ring;
R_j represents the amino acid side chain of Asn, Gln, Asp, Glu, Cys or Tyr;
and each of j, k, l, m, n, p and q is independently 0 or 1;
and the retro form, all D form, or retro all-D form of the peptide sequence of formula I, and salts and amides thereof.

61. (original) The method of claim 60, wherein the disease is any one of the diseases or conditions disclosed herein, preferably inflammation of airway epithelium, disorders of alveolar tissue, wounds, erectile dysfunction, urinary bladder incontinence, impaired hearing due to diseases of the cochlea, endothelial lesions, diabetic retinopathy and diabetic neuropathy, neuropathic pain, ischemia of the central nervous system, spinal cord injuries, dental tissue disorders including periodontal disease, kidney diseases, subchronic and chronic inflammation, cancer and failures of bone marrow or stem cell transplantation.

62. (currently amended) The method of ~~claims 52-61~~claim 52 or the method of claim 60, wherein the compound is represented by any one of the following formulae: (VII)



wherein,
R1 represents H or acetyl (Ac)
R2 represents a sidechain of one of the amino acids G, Y, D-Y, F and D-F,

R3 represents O or H

R4 represents any amino acid sidechain

R5 represents O or H

R6 represents a C(1-4)alkyl group, such as CH_2, $(CH_2)_2$, $(CH_2)_3$, and $(CH_2)_4$

R7 represents O or H

R8 represents O or H

R9 represents a sidechain of one of the amino acids G, Y, D-Y, F and D-F,

R10 represents OH or NH2,

and S, T, U, V and Z are integers defined as follows

S: 0, 1 or 2

T: 0, 1 or 2

U: 0 or 1

V: 0 or 1

Z: 0 or 1, or

R1-X1-X2-X3-R2
(VIII)

wherein,

X1 is 0, Ala, Gly, ß-Ala, Tyr, D-Tyr, Asp, HAA

X2 is 0; Ala-Gly-T4c-Pro; Ala-Sar-Hyp-Pro; Ala-6ring-; Ala-Asn; D-Asn-D-Ala; D-Asn; γAbu; Gly, Ala; D-Ala; ß-Ala; Pamh; Asn; or HAA;

X3 is Tyr; D-Tyr; Gly, Pamb, or Phe; and

R1 is H or Ac, with the proviso that X1 and X2 are not both 0;

and salts thereof.

63. (currently amended) The method of ~~claims 52-61~~claim 52 or the method of claim 60, wherein the half life of the compound as measured in a standard stability assay is more than 50 minutes and preferably more than 5 hours.

64. (currently amended) The method of ~~claims 52-61~~claim 52 or the method of claim 60, wherein the half life of the compound as measured in a standard stability assay is more than 5 hours.

65. - 89. (canceled)

90. (original) A pharmaceutical composition comprising a compound of general formula 1, formulae I to VIII , formulae 2 to 12, and the compounds of tables 1 and 8 or according to any one of the preceding claims, and a pharmaceutically acceptable carrier or diluent.

91. (currently amended) A composition according to ~~the preceding claim~~claim 90 which is an enteric tablet.

92. (currently amended) A composition according to ~~claim 89~~claim 90 which is an injection preparation.